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13. ABSTRACT

This symposium presents a survey of some of the allergy problems faced by the military population in their worldwide community. The titles of the ten articles reflect the scope of the symposium. The five pages of appendices provide some excerpts from Army Regulations and abstracts from the Veterans Administration schedule pretaining to physical fitness standards and rating allergic-type disabilities.

The titles of the articles are as follows: "Allergy in the military community", "Clinical allergy in air force medicine", "The management of atopic patients at sea", "Allergy in Thailand", "Atopy in Japan", "Exercise-induced bronchospasm in asthmatic patients" "Allergens and allergies at Fort Huachuca, Arizona", "Food sensitivity and military service", "Adverse immunizations reactions", and "Malarial antibody".

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PRESENT CONCEPTS IN INTERNAL MEDICINE

GUEST EDITOR FOR MAY 1971

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Presidio of San Francisco, California 94129

PRESENT CONCEPTS IN INTERNAL MEDICINE
VOLUME IV *May 1971* Number 5

ALLERGY
SYMPOSIUM

CONTENTS

FORTHCOMING SYMPOSIA . . .

RHEUMATOLOGY

PULMONARY DISEASES

FOREWORD

Allergy, and its allied field of clinical immunology, has shared in the renaissance of research immunology which dates from the publication of Colonel Bruton's initial report on hypogammaglobulinemia in 1952. In an attempt to obtain information on the beginnings of Allergy practice in Military Service, I recently wrote the S.W. French, III, Colonel, Medical Corps, United States Army, Retired. My reading had revealed that in 1954 his father had published an article entitled "Allergy in Military Service". It was the first publication in the first volume of the *Annals of Allergy*. With minor editorial changes Doctor French's reply is published below, and it is with pleasure that this issue of *PRESENT CONCEPTS IN INTERNAL MEDICINE* is dedicated to the first military allergist, **Sanford Williams French II.**

January 22, 1971

Dear Colonel McGerity

I was very pleased to receive your letter about my father and will attempt to give you some of his background, both civilian and military. . .

. . .Sanford Williams French II was born in Rochester, New York, September 12, 1881. He entered Cornell Medical School right after graduation from high school (no pre-med in those days). At the end of his first semester at Cornell, he was forced to drop out because of lack of funds. Another youngster (I've forgotten his name) was in the same predicament and the two enlisted in the US Navy -- this was early 1899 -- and both

were promptly shipped to Guam which had just been taken over from Spain as a result of the Spanish-American War. Dad was an "apothecary's mate" and spent two years on that island (one boat a month) eating rice and fish EVERY day. His duties consisted mainly of traveling throughout the island on an ox cart and giving the natives immunizations. He organized a stock company and produced "plays", had a pet monkey who was the nemesis of the whole garrison, and engaged in other activities to eat up the time – of which he had plenty. While on the island, however, he made some good contacts with officers of the Navy so that after his return to the States in 1901 and a re-enlistment, he was given an easy job as secretary to some Naval Board in Washington and had risen to rank of Chief Petty Officer. With the Navy's permission, he entered George Washington University Medical School in 1905 and graduated four years later – but he had promised the Navy he would enter the Navy as a regular officer upon graduation. He took the rigid entrance examination, passed it, but flunked the physical because of being underweight! The next chance to enter the Navy was one year hence so he explained to his superiors that he could not wait that long, particularly with a new wife, and asked their permission to try for the army. This permission was granted and two months later, after gaining weight on a diet of chocolate and olive oil, he entered the Regular Army.

In those days in the service, no formal training of any kind was offered and the specialists were self-trained men who finally achieved the general hospital circuit and were rotated from general hospital to general hospital. Dad never broke into the circuit so finally he asked for a year's training in allergy in 1924 at The Vandeveer and Cooke Clinic in New York — this was probably the first allergy clinic in this country. His request, naturally, was turned down so for the next three years he spent his leave time (he was stationed in Brooklyn) at this clinic, studying and

learning this new specialty of allergy. He also worked there many weekends. He was ordered to Fort Sam Houston in 1926 as Medical Supply Officer for then the 8th Corps Area and almost immediately after his arrival, by arrangement with the Commanding Officer of the Station Hospital (Brooke General Hospital was non-existent then), he established the Army's first allergy clinic and trained many young officers in this specialty. His interest in allergy never waned and even as Surgeon for the 4th Service Command during World War II he established many allergy clinics and even hit TIME Magazine with his poison ivy extract. He was a great man, a great father, and a great physician, and I will remain eternally proud of him and his accomplishments against almost overwhelming odds. He was retried from the service late in 1944. After retirement he established an office in his home in San Antonio, and was quite active in his field until several years before his death , August 21, 1957.

Sincerely,

(signed) *S. W. FRENCH, III, M.D.*

> . . .the 'clinical immunologist' in general would be expected to deal with: diagnosis where this can be assisted by immunological techniques; prophylaxis and treatment by immunological methods; management of conditions in which immunological mechanisms are implicated and where their modification may be beneficial; and disorders of the immunological system itself.

Pepys, J. 'Clinical immunology' and the 'practice of allergy'. *Clin Allerg* 1:1-7, 1971

ALLERGY IN THE MILITARY COMMUNITY

LTC Joseph L. McGerity, MC

Allergic disorders pose a problem of considerable magnitude to the medical service of the military in the evaluation and diagnosis of individuals being considered for entrance into the military service and in the evaluation, diagnosis and treatment of those on active duty, their dependents, and the retired population. There are both administrative and therapeutic considerations which are unique to these groups. However, in addition to these problems, there are unique opportunities for the allergist in this setting.

Estimates of the presence of atopy in the civilian population at some time during their life have varied from ten to twenty percent, and an estimated five percent of the population are, have been, or will be suffering from asthma. Because medical requirements for entrance into the military tend to select males without allergic disease, it might be postulated that there would be a smaller incidence of atopic disease both in active duty personnel and in their children. No statistical studies are available for the incidence of atopic disease in either active duty military, their dependents, or the retired population. The demand for the services of an allergist are evident to any military physician and the need appears to be increasing. This increasing demand for service has also been evident in civilian practice and may merely reflect increasing sophistication of the population or may truly indicate increasing distribution of the genes controlling atopic conditions.

The military services are in a favored position in that they can select through the armed forces examining stations those individuals who will have the least predisposition to atopic disorders. Appendix I lists the pertinent sections

of Chapter 2, AR 40-501, for atopic disorders which are considered disqualifying for appointment, enlistment, and induction into the military service.

One of the more difficult regulations to interpret is paragraph 2-39a.(5), AR 40-501, dealing with generalized reactions to insect bites or stings. To a large extent the history is dependent on the subjective interpretation of symptoms by the patient. We have tended to require documentation by a physician of such an episode unless the history is entirely consistent with this diagnosis. Skin tests are often of little value in confirmation of this disorder.

Paragraph 2-26b, dealing with bronchial asthma is subject to various interpretations. Many examining boards in the past have interpreted the phrase "with a trustworthy history of freedom of symptoms since the 12th birthday" to indicate that the candidate for entrance into military service must present written documentation from a physician of wheezing after the age of twelve. This has been particularly true for inductees. However, when considering enlistees, they have made little attempt to investigate the patient's history to confirm that he has not had symptoms after the 12th birthday. In evaluating these patients with a history of significant childhood asthma who present at this clinic, we tend to place the burden of proof of freedom from asthma after age twelve on the individual. A phone call to the family physician has resolved many problems quickly.

Because of the varied interpretations of paragraph 2-26b, and excessive zeal of many recruiting personnel, persons with disqualifying bronchial asthma have been enlisted in the military service. Regulations require that an individual with a condition which would have permanently disqualified him for induction under Chapter 2, but does not disqualify him for retention under Chapter 3, AR 40-501, must apply for release on the basis of this condition within 4 months from the date of initial entry on active duty - information which is not likely to be widely disseminated in training centers.

As a result of the pressure of training requirements and a shortage of trained allergists at basic training centers, many of these individuals complete four months of military service before their condition comes to the attention of the

medical service. At that time their condition can not be considered disqualifying for military service under paragraph 25, Chapter 3, AR 40-501, yet it is obvious to the medical personnel concerned that these patients will not do well in military service and that their retention will be detrimental to the patient and a liability to the government. In such cases medical judgement should be exercised by the Board considering the case under paragraph 3-36c, AR 40-501.

Members of the National Guard of the United States and the Army Reserve not on active duty are frequently referred to Allergy Service for evaluation of their fitness to remain in a non-active component because of conditions of an allergic nature which have developed during their service in these units. These individuals are evaluated under Chapter 3, AR 40-501, and at times it seems incongrous that they are to be considered fit for service whereas their civilian counterpart would not be considered fit for induction into the military service. When in our medical judgement these medical conditions appear to be of progressive severity, approaching a point of disqualification under Chapter 3, these patients are considered under the provisions in that chapter of AR 40-501, paragraph 3-36d. One of the problems of considering National Guard and Reserve personnel under Chapter 3 is that while patients on active duty who are considered under this regulation are furnished the facilities for proper treatment of their condition within the military service, this treatment is not available to those personnel not on active duty.

As a medical facility serving as a consultant service to a port of embarkation for the Far Eastern area, we are frequently called upon to evaluate an individual's medical fitness for duty in Viet Nam or Korea. In our experience most persons with allergic rhinitis do surprisingly well in either theater and it has been our policy not to place geographical restrictions on such individuals, but to recommend that they be assigned duties where they may continue to receive hyposensitization (if this has been instituted). If sneezing or severe conjunctivitis has been a major problem, a profile recommendation is made to preclude assigned duties where sneezing would expose either the individual or his unit to hostile fire or where compromise of his vision by an allergic reaction would impair his performance of duty. These individuals

are not restricted from field duty assignment as it is considered that their major restriction would only limit them from participating in patrol duties or search and destroy missions. In our experience patients with atopic eczema do not do well in Vietnam and patients with bronchial asthma do not do well in Vietnam or Korea. These patients are considered under AR 40-501, Change 15, paragraph 7-9, and in those instances where there is a reasonable doubt as to the propriety of assigning an individual to Southeast Asia from either a productive service or a medical management standpoint, he is considered by a medical board to determine an appropriate disposition.

Appendix II outlines those provisions dealing with allergic diseases in Chapter 3, AR 40-501. Medical judgement must be exercised in the interpretation of paragraph 3-25a, dealing with retention of personnel who have bronchial asthma. First, it is well recognized by allergists that emphysema per se is not a complication of asthma. It is also recognized that pulmonary function studies may be entirely normal between attacks of asthma. Therefore, we base our evaluation of the severity of the patient's asthma on the time lost from duty, requirements for medical care and hospitalization and his need for steroids. In our evaluation of the relationship of steroid therapy to the severity of asthma, we tend to evaluate steroid usage from the viewpoint of the possible effects of this medication. If there is no evidence of metabolic derangement with steroid therapy, or if the patient is controlled on doses (once in the morning, short courses of steroids, every other day steroid therapy) such as to preclude adrenal suppression, the use of steroids alone should not be considered disqualifying. The evaluation of asthma requires utilization of all available knowledge of the latent potential of this disorder, the possible adverse effects of therapy, the value of the individual to the military service, and possible adverse effects of service upon the individual.

The Allergy Service has been called upon by the local physical evaluation board for guidelines in rating asthma at the time of retirement evaluation. Appendix III gives Veterans Administration (VA) rating codes for allergic conditions. A major problem of the rating system for asthma is the requirement that emphysema be evident for a rating of anything but "mild". As previously mentioned, emphysema is

not considered a consistent or even commonly associated condition in asthma and pulmonary function studies may be entirely normal between the characteristic episodes of asthma. Yet, asthma is a potentially fatal disease, often causes prolonged absence from work and limits the type of work that can be performed. It requires frequent medical visits and often frequent hospitalization, and if the asthma is allergic in etiology, it requires limitations of certain social activity, changes in the household environment, and frequently repeated medical office visits for hyposensitization therapy. All of these restrictions on the normal life of the individual can occur with no evidence of emphysema and yet require treatment (hyposensitization, steroids, etc.) which is not without risk. Thus, the asthmatic patient does not readily lend himself to a grading of his disability on the basis of a pulmonary function impairment which may be entirely absent at times, present only under certain conditions to varying degrees, or present at particular times to such a degree that he is disabled for the minimal activities of daily living.

The problems faced in treating dependent personnel of the pediatric age group and the retired population are in general those present in the civilian community. A difficulty does arise in planning for the care of these patients over an extended period of time, because it is difficult to estimate the size of the dependent population due to fluctuations caused by unit transfers, rapid mobilization or demobilization, and the population shifts that determine the retirement location of many personnel. In fact, reliable statistics are not available on the static location and service density of this population group at any one time. Because of rapid population shifts with non-availability of military personnel trained in allergy, liberal use of the Uniformed Services Health Benefits Program may be indicated. Due to the chronic shortage of medically trained personnel throughout the economy, this resource may not be available at times.

Among the unique problems in the care of a military population is the rapidity with which these families are shifted from one environment to another with changes in exposure to pollens and other inhalants, temperature variations, altitude, smog and dust (Yokohama Asthma) and the

psychic changes associated with moving, separation from the family head, and changes of physician. This, however, in our rapidly changing society is also becoming true of the civilian population. Continuity of care of allergic conditions is an important factor. Repeated evaluations are often necessary for elicitation of precipitating factors, for evaluation of therapeutic procedures (particularly hyposensitization), and for the establishment of rapport between the physician and patient in a condition such as asthma where anxiety often accompanies the disorder.

For those patients on hyposensitization, change in location may lead to early discontinuation of such therapy. However, current policy at Letterman and Walter Reed General Hospitals permits these installations to furnish extracts to patients anywhere in the world. It is our policy to furnish the extract on the request of a physician or medical installation. We hesitate to change the hyposensitization program of any patient until they have lived in our area of responsibility for at least one year, and it has become evident that they are reacting to allergens not previously recognized and/or not included in their previous hyposensitization extracts. Some physicians have tended to discontinue hyposensitization because the extract contains an antigen, such as ragweed, which is not prevalent in the new location. We do not accept this philosophy unless it is fairly certain that the individuals or his family's future assignment will not involve a return to an area where this antigen is prevalent.

The fact that our patients are often referred from rather isolated dispensaries with changing medical personnel imposes certain restrictions on hyposensitization, such as very conservative injection schedules. Hyposensitization is begun at extremely low dosage and increased by very small increments. At no time are patients furnished this mode of therapy unless it will be administered where a physician is <u>immediately available</u> for treatment of any adverse reaction.

A persistent shortage of physicians trained in allergy exists both in the military and civilian community. At the present time military allergists are obtained from civilian sources, from civilian training centers through the influence of the selective service program, from the "Berry plan", from military physicians who have obtained their allergy training at civilian institutions and are therefore obligated

for prolonged tours of duty, and through the allergy residency programs at Walter Reed and Fitzsimons General Hospitals. These programs have not resulted in significant retentions of military allergists because the obligatory service time has been short and the economic competitions from the civilian community has proven too tempting to many of these physicians.

Because allergists in the military service are most often assigned to general hospitals serving a wide geographical area, it takes months or years for them to appreciate fully the significance of the varying climatic, flora, and other environmental conditions of the widely diverse locations where the military population lives. Stability of tours of duty permits full utilization of accumulated knowledge.

A very real problem faced by the military allergist is the frequently changing personnel situation in the clinic. Medical corpsmen assigned to an allergy service require specialized training in skin testing and in the preparation and the administration of hyposensitization extracts. Since there is no special MOS awarded for this training, these personnel are considered in the general pool of medical corpsmen for reassignment. A more satisfactory scheme has been the utilization of civilian personnel for nursing and technical duties in large allergy clinics.

For many years the allergist was not recognized by many of the medical community as a "respectable" member. Only with the advent of immunology into general medicine and the recognition that antibodies can be responsible for disease has this attitude changed. Certain medical schools only recently recognized the legitimacy of the subspeciality of allergy. Their graduates and those of previous years from other schools are now entering the military service for short tours of duty. The predetermined attitudes of these physicians, particularly when they are stationed at isolated locations, poses certain problems for the allergist. There is a tendency for these individuals frequently to regard allergic conditions such as asthma and urticaria as a manifestation of a psychoneurosis and to reflect this attitude in their response to the patient and the program outlined for his care by the allergist. These same individuals tend to be uncomfortable when required to treat the asthmatic patient. Because of

their previous training they are unfamiliar with the potentials for improvement in certain patients with hyposensitization and with the dangers of this mode of therapy. Because of this lack of familiarity with hyposensitization, necessary precautions may not be observed.

Allergy practice in the military service can be a rewarding experience. This is evidenced by the enthusiastic interest of most of those now practicing this specialty in the service. The service is unique in that clinical allergy can be practiced on a rational basis with little regard for personal economic well-being. Laboratory studies that the patient requires are readily available and consultations from other specialties are easily obtained. The opportunity for clinical investigation of such problems as immunization reactions, drug reactions, and the efficacy of various modes of hyposensitization exist. The military allergist usually works with a young, well-trained, enthusiastic group of associates and has teaching as well as research opportunities.

This positive approach has been emphasized at recent meetings of the allergists of the three military services. An Association of Military Allergists is being organized under the chairmanship of LTC James E. Shira of Fitzsimons General Hospital. It is hoped that the Association can contribute to the care of the allergic patient by dissemination of information to civilian colleagues regarding regulations for induction and the documentation needed from civilian physicians, and by participation in certain study committees of the Academy of Allergy through such unique opportunities as the ability to investigate world-wide environmental allergens. Within the group, information will be disseminated on regulations, hyposensitization programs, and environmental factors present at various locations where military personnel are stationed.

CLINICAL ALLERGY IN AIR FORCE MEDICINE

LTC Ned J. Whitcomb, USAF, MC*

The following comments are based on experience obtained in the past three years as Chief of the Allergy Service at the David Grant USAF Medical Center at Travis AFB, California. This is not intended to be an exhaustive report, but rather an insight into where an allergist and clinical allergy fit into the overall picture of Air Force Medicine.

An allergy practice in the Air Force is much like that of civilian life with a few exceptions. Vaccine hypersensitivity is an important area that rarely confronts the civilian allergist but is an everyday problem in an Air Force Allergy practice. The major disease processes that are diagnosed and treated specifically by the allergist are pollinosis, or seasonal allergic rhinitis, perennial allergic rhinitis, and allergic bronchial asthma. Implicit in this is the differentiation of these illnesses from others such as vasomotor rhinitis, foreign body aspiration, emphysema. There is a tremendous overlap of clinical allergy and immunological problems into most areas of medicine. It is probably true that systemic manifestations of allergic disease involve all systems and only our lack of sufficient knowledge prevents clear-cut demonstration of this. For this reason, medical board evaluation often requires an allergy consultation. Frequently encountered problems that involve other medical specialties would include drug hypersensitivities, dermatitis (atopic or immediate hypersensitivity; contact or delayed hypersensitivity), urticaria, both acute and chronic, gastrointestinal symptoms, and immunological deficiency diseases associated with hematology or oncology.

There are allergic disease symptoms which prevent eligibility for Air Force duty. These requirements become more stringent for flying jobs and most restrictive for application

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to the Air Force Academy. Once an individual is on active duty and the Air Force has invested time and money in his training, he may be retained for active duty, assuming his allergic symptoms are controlled adequately. Rejection for enlistment in the Air Force would occur if the candidate has allergic rhinitis, unless it is mild and controlled by medication or hyposensitization, An applicant for pilot training or for the Air Force Academy is rejected if there is any substantial history of allergic rhinitis unless free of all symptoms from 12 years of age. The use of words "mild" in the former and "substantial" in the latter case gives flexibility to the regulation (AFR 160-1, pages 85 and 86, para. 60). In the case of allergic asthma, Air Force regulations state that it will be a cause for rejection for enlisted men or officers if present in any degree or if there is any history of asthma except a history of childhood asthma with a trustworthy history of complete freedom from symptoms since the twelfth birthday. (AFR 160-1, page 93, para. 76). The question of a trustworthy history will always be a doctor's dilemma. Some candidates for the Air Force fail to include asthma on their medical history forms for a variety of reasons. This results in a large number of clinically symptomatic allergic people on active duty. Of course, there are those individuals who develop allergic symptoms for the first time after entering the Air Force, but these are rare and often quite difficult to manage.

The management of flyers is a particularly difficult problem since flying is not permitted if medication has been taken in the previous 24 hours. The allergic patient on flying status may not take antihistamines as may his counterpart on the ground. If such a patient can be successfully managed with allergy therapy, he may be granted a waiver for his allergic disease according to current Air Force policy. His therapy will usually include environmental control and allergy injection therapy. The School of Aerospace Medicine at Brookes AFB in Texas is currently evaluating some antihistamines to see if flying people can safely use them.

Each branch of the military has different regulations regarding immunizations. Air Force requirements are that all active duty personnel be able to perform world-wide duty. The World Health Organization requires valid international certificates for smallpox, yellow fever, and cholera immunization.

Therefore, any active duty Air Force person must meet a medical board and face possible discharge if he cannot receive any of these three immunizations. The most common clinical problem is the patient who is sensitive to egg protein. The yellow fever vaccine contains this protein. Other egg-based vaccine immunizations may be waived by request through proper Air Force channels. (AFR 160-13, page 3, para. 9). The other egg-based vaccines are typhus, influenza and measles.

There are problems surrounding successful environmental control measures in USAF barracks. Usually a simple verbal request by the patient is sufficient, but on occasion the first sergeant will require one or more letters of authority to put on a mattress encasing or close off a forced air heat vent or remove a piece of furniture. All Air Force pillows are made of feathers and usually need to be replaced at the expense of the patient.

Allergic patients who are on flying status have irregular hours and find it difficulty to follow any regular schedule of injection therapy. With proper motivation, these patients will work up to a maintenance dose which can then be given every three to four weeks. Some negative motivation may be the fear of being grounded and losing flight pay.

Allergy injections are given in Southeast Asia. Few inhalant allergy patients experience allergy symptoms in Southeast Asia due to the unusual pollens present there. These patients are in an ideal situation to receive their immunizing injections in the absence of airborn allergens in their environment. When these patients then come back to the United States (CONUS), they have high levels of immunity and generally experience diminished allergic symptoms.

There are many "allergy clinics" in the Air Force that are strictly "allergy injection clinics" - they do not have a trained allergist and may not be the assigned responsibility of any physician. The technician giving injections may have a very good background in allergy or have had only two weeks of training. This situation may be relieved in the future if the Air Force's current plan for a physician's assistant program is carried through to the subspecialty services. There will never be enough trained allergists to adequately handle all the

allergy clinics in the Air Force and a well-trained physician's assistant could fulfill this need.

The Air Force specialty code number for allergy-immunology technicians is 912X4. The administration of routine immunizations is part of the job description. This is unfortunate since a medic at the lowest level may quickly become competent in administration of routine immunizations. However, a skilled allergy-immunology technician may be assigned to this area and be completely out of his major field of training. An allergy-immunology technician who is assigned to an allergy clinic may not have had any experience in actual allergy work if his prior assignments were in routine immunizations only. To further complicate the problem, this skill field is considered critical; however, there are no new 912X4s currently being trained in the Air Force.

The proper utilization of allergists has not always been possible in the Air Force. This stems from the two types of training programs which lead to being a subspecialist in allergic disease. One must be certified in Pediatrics or Internal Medicine before being eligible for formal training and certification in Allergy. On more than one occasion it has been found necessary to assign a fully qualified Pediatric Allergist to a base as a general pediatrician. This problem was recently discussed by the Section of Military Allergists at the American Academy of Allergy.

Most allergy training programs now have a mixture of pediatric and adult patients. Therefore, the clinical allergist, supported by pulmonary medicine and pediatrics can intelligently deal with the clinical allergy problems of both active duty and dependent patients.

The future practice of allergy in the Air Force could be markedly improved and simplified if certain changes were to occur. Some of these would include: uniformity in allergy extracts - possibly with a central laboratory for extract production for all of the Armed Forces or at least for the Air Force; assignment of fully trained allergists to regional medical centers rather than satellite bases; use of physician's assistants for allergy clinics with close support by regional medical centers; greater awareness of hospital commanders for the need to have adequate allergy care for their patients; and, more liberal use of CHAMPUS for severe but uncomplicated and routine allergy problems.

THE MANAGEMENT OF ATOPIC PATIENTS AT SEA

Captain R. H. Barrick, MC, USN*

Therapeutic principles for the treatment of patients with allergic diseases are, in general, universal, consisting of avoidance of known symptom-producing antigens, environmental control, drugs, appropriate immuno-therapy, and psychiatric assistance if needed. These modalities on occasions have to be altered in situation encountered by patients who are mobile and transient such as those on sea duty.

The purpose of this paper is to furnish the military physician information regarding the type of illnesses common to the atopic patients at sea and suggestions for their medical management.

Respiratory diseases comprise a major portion of the illnesses involving personnel stationed aboard ships of the United States Navy. Epidemiology studies of a cruiser complement indicated 15-26 percent of all illnesses were respiratory in origin. The incidence of Allergy (IgE-mediated) as an etiologic cause of such illness would be speculative because no such extensive study has been reported. Cumulative experience at four Navy Hospitals which are referral centers for the fleet on the east and west coasts and from reviewing medical boards of Navy personnel with the diagnosis of asthma over a two-year period indicates that allergic individuals with perennial rhinitis exacerbated by nonimmunologic mechanisms comprise the highest percentage of the atopic population seeking treatment at sea. The reasons for this are multiple.

- Physical qualifications for entrance into the armed forces not only restrict applicants with active asthma, atopic dermatitis, severe rhi-

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nitis and bronchitis, but also stringent physical standards are imposed on candidates from the Navy who seek commissions or positions in aviation, diving, and duty on submarines.

-- Personnel with asthma, recurrent bronchitis, and chronic rhinosinusitis are ordinarily immediately transferred when possible from ships or sea-going billets to medical centers for complete evaluation, treatment, and disposition as soon as these diagnosis are entertained. Since these illnesses are associated with significant loss of man-hours from work, vacant duty stations and lower efficiency of the ship's operation, prompt action is necessary so as to permit early replacement of personnel. To the medical department, these illnesses represent a constant threat for overloading a small staff, problems in treatment and depletion of limited medical supplies.

-- Prominent immunologic factors which precipitate allergic illnesses ashore, such as antigens from pollen, non-pathogenic fungi, animal danders and house dust, are either absent from aboard ship or progressively diminish in concentration at sea to become clinically insignificant. The excention to this might be house dust exposure for certain individuals such as the compartment cleaners and members of the deck force.

-- Nonimmunologic conditions known to have adverse effects on the respiratory tract are encountered frequently in the ship's environment, E.g. exposures to wide variations in temperature, fog, wind, paint fumes, stack gas, petroleum products, jet blasts, cigarette smoke and other factors conducive to vasomotor rhinitis. These "other factors" include long working hours, irregular sleeping patterns, confining living quarters, prolonged absence from family and loved ones, and certain situational stresses beyond individual control.

The medical staff on board ship at sea may be small in number, and it consists of trained paramedical personnel with or without physicians depending on the class of the ship and the size of the ship's crew. These criteria also regulate the financial budget and the physical spaces allotted for medical care, supplies and equipment. Laboratory facilities are available only on relatively few vessels, and with the exception of hospital ships, only basic tests can be performed.

In the management of allergic patients at sea, the diagnoses of illnesses are made primarily on the history and physical findings by physicians or paramedical personnel. Medications are confined to elementary drugs such as epinephrine, aminophylline, chlorpheniramine, diphenhydramine, triplenamine, pseudoephedrine, prednisolone, hydrocortisone ointments, and usually three different antibiotics. Hyposensitization injections or immunotherapy are administered only when a physician is in attendance and then at his discretion. Prolonged systemic corticosteroids regardless of schedule are not considered appropriate for individuals aboard ships without a medical officer. With the surveillance of an on-board medical officer low dose or alternate day systemic corticoids may be acceptable.

Military physicians at shore installations are often consulted by the medical staff on board ships for advic regarding diagnoses and treatment of their patients. In such instances when the patients have allergic illnesses consideration of the conditions aboard ships by the consultant will enhance the medical care of the patient and consequently facilitate the ship's operation. If medications or therapy other than that which is immediately available are needed or if there is question regarding patient disposition, direct communication with the medical department representative is urged for quick resolution of the problem.

In summary, personnel on sea duty are as a group are healthy because of predetermined physical qualifications. Perennial rhinitis aggravated by nonimmunological stimuli is believed to be the most common illnes affecting the atopic population at sea. The methods of treatment of allergic illnesses at sea are governed by the availability

of physicians, paramedical personnel, medical supplies and facilities.

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ALLERGY IN THAILAND

LTC Frank K. James, Jr., MC*

Just as diseases endemic to the tropics have challenged military physicians, so do the unusual manifestations of allergy seen in Southeast Asia. Atopic military personnel stationed in these areas encounter problems rarely experienced in the continental United States. Respiratory symptoms are influenced by continual pollination of grasses and weeds, so that classic seasonal pollinosis is not seen. By contrast, personnel have often encountered molds in extremely high concentration; and in the environs of Saigon and Bangok they have faced atmospheric irritants or pollutants common to large industrial areas. Dust has been a major problem in some areas.

The Army's principal mission in Thailand has been logistical. This has included completion of a huge port complex at Sattahip, several military installations, and a road system leading from the port area to northeastern Thailand. Atopic personnel assigned to the port area have experienced severe respiratory distress from high dust concentrations, often they have required change in assignment to other areas of Thailand or medical evacuation out of country. Road building crews have encountered similar problems, but not of the magnitude encountered around Sattahip.

An understanding of the topography and climate of Thailand helps to clarify some of the respiratory problems allergic patients have encountered in that country. Thailand lies between 5 and 21 degrees north latitude, and 97 and 100 degrees east longitude. It is a country of approximately 200,000 square miles, about four-fifths the size of the state of Texas and is elongated and irregular in shape, extending 1300 miles north to south, and 500 miles east to west.

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Thailand is characterized on the north by forest covered mountains and foothills, in the center by high plateau and on the south by flat alluvial plains which are intersected by winding rivers and streams and become inundated during the monsoon seasons. Bangkok lies in the alluvial plains to the southwest.

The Korat plateau is located in central Thailand, 100 miles northeast of Bangkok. The somewhat arid section of Thailand is separated from Bangkok by a small chain of mountains rising some 2,500 feet. South of the Korat plateau near the Gulf of Thailand lies the great Central Plain where most rice is grown.

Thailand is under the influence of seasonal monsoons. In the northeast the mildest time of the year is from November through February while March and April are ordinarily the hottest times of the year with temperatures usually exceeding 100 degrees Fahrenheit. With the onset of monsoons (usually in September), relative humidity rises, and the temperature remaining about the same. In southern Thailand, particularly around Bangkok, there is a double rainy season. The first is from May through October when monsoons arise from the southwest and the second from November through February when monsoons come from the northeast. Rainfall in the Bangkok area averages greater than 150 inches per year compared to the northeast where rainfall averages less than 50 inches per year.

The relative humidity in northern and central Thailand ranges from 30 to 60 degrees in November through February. Humidity commenses to rise during the late summer and early fall months. In the alluvial plains around Bangkok, relative humidity remains high and average temperature are greater than 90 Fahrenheit the year around.

With this variety of climates and topography, local environmental factors tend to influence allergic respiratory disorders. There appears to be an increase in respiratory infections coincident with the monsoon seasons, similar to that noted during the colder and wetter times in the continental United States. One local allergist in Bangkok thinks that there is a direct correlation with "bacterial allergic patients" who have most of their

respiratory distress during the monsoon seasons. These have been treated with an autogenous bacterial vaccine, and for severe respiratory infection with appropriate antibiotic therapy.

The local populus is also affected during the rice harvesting season with an increase of respiratory problems, usually characterized by severe bronchospasm. This appears to be somewhat akin to dust hypersensitivity and may involve mites as antigenic factors. This problem has yet to be fully defined.

Coincident with the monsoon season, and increased relative humidity, mold spore counts are extremely high and mold sensitive patients have their worst symptoms at this time of the year. Pollen counts and identifications, along with mold spore identifications have been identified only in the immediate Bangkok area. Initial studies have been completed around the city of Korat.

Insofar as pollens are concerned, there is an abundance of grass around Bangkok and in southern Thailand around the Gulf of Siam. Grasses most commonly identified as being antigenic are usually bermuda or timothy grass. Trees, particularly in the Bangkok area, are tropical. Weeds, characterized by cocklebur, spiny amaranth, goldenrod, and plantain, are in abundance in many areas of Thailand. There appears to be little ragweed. Weeds do not appear to be a major antigenic problem either among the local populus or the military assigned in Thailand.

The most common molds identified are Alternaria, Phoma, Hormodendrum, Aspergillus, Mucor, and numerous Penicillium species. Molds abound in most areas of Thailand but especially around Bangkok. Immunotherapy for mold sensitive patients appears to be successful.

A surprisingly large number of atopic patients with severe respiratory infections were noted in a year of study in Korat. Patients with mixed allergic and infectious asthma required vigorous medical support and on some occasions were medically evacuated from Thailand.

Other than Bangkok and immediate environs few detailed studies of environmental factors and allergens have been completed. During the one year assignment in Korat, pollen studies were initiated and some identified. Careful histories, complete physicals, selected skin testing and appropriate supportive therapy gave good results, however, much is yet to be learned in Thailand, as well as Southeast Asia.

ATOPY IN JAPAN

COL Robert E. Smith, USAF, MC*

With the exception of two problems, the practice of allergy in Japan is surprisingly similar to the practice of allergy in various areas of the continental United States. The two problems are (1) lack of a comprehensive survey of the allergens in the area, and (2) a specific air pollution bronchitis called Tokyo-Yokohama asthma (T-Y asthma).

ALLERGENS

As of this writing I have been unable to obtain a survey of the common allergens anywhere in the Japanese islands and particularly in the Tokyo-Yokohama area or Kanto Plain area. The Kanto Plain area is a wide tract of land on the eastern coast of Japan bounded by mountains on the north and west and includes the metropolitan areas of Tokyo and Yokohama. Casual observation in the area shows one that the area has a great deal of grass which appears to be of the same varieties that occur in other areas of the world. In addition, of course, there is a great deal of rice grown in the area, but how much, which ones, if any of the rice products in the area cause allergic problems has not been determined. Also, most Japanese homes have tatami mats made from a straw fiber which obviously breaks down and creates dust which has antigens common to most of the grasses. There are several varieties of weeds in the area, among which I recognize franseria and amaranth. I have not found any ragweed as yet.

Among the large variety of trees are members of the elm, ash, hickory, and oak families. House dust is as common an antigen here as in the United States and the only difference noted has been the addition of grass antigen from the tatami

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mats. Mold growing in various areas of the houses, e.g., bathroom and kitchen, is readily noticed in the majority of homes. In addition, mold is prevalent outside and seems to be much the same seen along the eastern seacoast of the United States.

Therefore, in generalities, the allergens appears to be much the same in Japan as in the United States, however, these are gross observations and are not based on comprehensive allergy surveys either from botanical recognition or pollen counts.

TOKYO-YOKOHAMA ASTHMA

About 1946, shortly after World War II, some United States military personnel stationed in Yokohama, Japan began suffering from sudden attacks of wheezing, coughing, and dyspnea. Attacks occurred mainly at night, particularly in the early morning hours and were most likely to occur in the fall and winter. Relief came promptly when the patients left the Yokohama area and recurred only if they returned. These were the earliest observations on a disease which has come to be known as the "Tokyo-Yokohama asthma". The clinical manifestations of T-Y asthma have been nearly identical in all patients and the description of the symptoms to follow in our patients are essentially unchanged from those described in earlier papers. /1-4/ Symptoms appear in the late fall and early winter, abate during spring and summer, and recur the following fall. Most individuals become ill the second year after arrival in Japan. Some persons, most notably those who have had a previous tour of duty in the Kanto Plain area, experience symptoms the first year.

Nocturnal cough is usually the initial complaint, followed by wheezing and mucoid sputum production; nasal stuffiness frequently accompanies the wheezing, but sneezing, rhinorrhea, skin rash, and burning eyes are usually absent. Symptoms reach a peak in the late afternoon and evening hours, and become less intense during the late morning and mid-day. Coughing and wheezing increase on days when air pollution is

heaviest and air movement is limited by thermal inversion and low surface wind. Patients leaving the area for temporary duty assignment or vacation experienced complete to moderate relief of their symptoms. Return to the area usually induces an almost immediate recurrence of symptoms. None of our patients have noted a history of recurrent pneumonia or chronic sputum production. A "cigarette cough" is infrequently admitted even among heavy smokers. Approximately one-half of the patients give a personal history of allergy or know of a family member with hay fever or asthma, but most patients have not experienced an asthma attack before their arrival in Japan. Most of the patients are heavy smokers, smoking in excess of one pack of cigarettes per day. However, cessation of smoking fails to arrest symptoms in any of the patients although coughing frequently is noticeably diminished.

A statistical comparison of mean eosinophil counts between patients with T-Y asthma and routine surgical patients reveals that the T-Y asthma patients have an elevation of blood eosinophils which is highly significant. /5/ Sputum smears for the presence of eosinophils is usually positive in the T-Y asthma patient. Pulmonary function testing consistently demonstrates airway obstruction.

During the acute state of the illness the 0.5 sec ($FEV_{0.5}$) and 1.0 sec ($FEV_{1.0}$) forced expiratory volume, the maximum breathing capacity (MBC), and the mid (MEFR) and maximum midexpiratory flow rate (MMFR) are consistently below predicted value. In the summer months the pulmonary functions significantly improve. However, they usually remain abnormal in comparison to the mean value of healthy subjects.

Intradermal skin testing to a variety of allergens including pollens, molds, house dust, epidermals and fibers (which include tobacco) have shown no correlation to the symptoms of T-Y asthma. This has been the experience of previous investigators also. Chest roentgenograms taken during peak symptomatology failed to reveal any significant abnormality.

T-Y asthma has been attributed to the dense air pollution present in the Kanto Plain area of Japan. The evidence for this has rested in the reported studies of Smith et al /1/ and Beard

et al /6/ who had best shown a correlation of symptoms with the level of air pollutants and meteorological conditions which gave rise to dense air pollution. Frequently occurring states of thermal inversion trap air in the lower atmosphere and these thereby raise the density of air borne particles. These conditions occur most frequently during the fall and winter months. Although air pollution levels have not been measured in association with our patient's symptoms, the association of symptoms with smog formation was clinically evident. However, it is to be noted that the thermal inversions and thick smog occurring in summer months are associated with only minimal symptoms of T-Y asthma or not at all.

The persistent finding of blood eosinophilia and a high incidence of sputum eosinophilia suggest an allergic or hypersensitivity mechanism. Conceivably T-Y asthma patients may be mildly atopic individuals who require chronic or maximum exposure to the particular air pollution antigen before symptoms become manifest. Popa et al /7/ have reported asthma following exposure to simple industrial chemicals such as ethylenediamine, sulfathiazole, and chloramine. He has postulated several different mechanisms in the etiology of asthma following exposure to these simple industrial chemicals. An allergic etiology for T-Y asthma has been postulated by Spotnitz /8/ but the responsible allergen has not been identified by him. He believes that most patients were allergic individuals who happened to acquire their asthma while living in Japan. Haycraft /9/ suggested that T-Y asthma was secondary to viral respiratory infections which commonly occur during the fall and winter months. There has been no evidence of a herald infection in our patients. Certainly many of the patients became more symptomatic during episodes of respiratory infection, but these are easily recognized as such.

The clinical features and laboratory findings of eosinophilia in T-Y asthma would be most adequately explained by an allergic mechanism to an air pollutant such as that demonstrated by Popa et al /7/ to ethylendiamine. Periods of peak air pollution are found in the fall and winter months at a time when most T-Y asthma patients note the onset of illness and peak symptomatology. The presence of some air pollution throughout the year would also explain

the persistence of airway obstruction in many of the patients during the summer months (improved stage). Recurrence of symptoms on return to the area also suggests an allergy to a specific antigen. At the present time, however, no specific allergen can be incriminated.

An undefined factor has been the role of cigarette smoking. Cigarette smoke has been known to increase airway obstruction even among normal subjects. /10/ This irritative effect could induce symptoms of wheezing in an otherwise mild or asymptomatic individual. Conceivably there could be a common allergen shared by air pollutants and cigarette smoke. At any rate, the rarity of the disease in children and non-smokers points to a rather close relationship between the disease and cigarette smoking.

TREATMENT

The treatment of T-Y asthma is much like the treatment of other forms of allergic asthma and is approached in two phases -- (1) the treatment of the acute attack and (2) the long-term or prolonged treatment of the illness. The immediate treatment consists of epinephrine either aqueous or long-acting, fluids, aminophyllin and intermittent positive pressure breathing. The long-term management of the patient consists of symptomatic therapy with sympathomimetics and theophollin derivatives, expectorants, cessation of smoking, and early rigorous treatment of any secondary infections. Approximately half of the patients with T-Y asthma become refractory with these simple medications and require the use of steroids. Adverse effects of isoproterenol inhalation therapy has been frequently seen by us and attributed to the repetitive use of inhalation nebulizers for treatment of chronic wheezing. Rebound obstructive phenomenon after isoproterenol inhalation has been previously reported by Kaplan et al /11/ and implicated by Spiezer /12/ as the cause of increased asthma mortality. It is our practice to discourage the use of hand nebulizers in all cases of asthma.

Once the patient has developed T-Y asthma the only way to completely control his symptoms is remove the patient from the Kanto Plain area. As mentioned above about half of the patients with the disease can be controlled with simple medication for a year or two. However, once a patient becomes refractory to routine symptomatic therapy and requires

steroids the disease usually becomes progressively more severe. If the patient is removed from the area in a relatively early stage the disease seems to clear rather quickly. However, some patients who have been maintained in the area for long periods of time with the disease do not become symptom-free for many months after leaving. In the past two winters three patients with T-Y asthma who had refused or resisted being removed from the Kanto Plain area for one reason or another have died of the disease. Since there does not appear to be any exacerbation of the disease from smog any other place in the world and because of the dangers associated with remaining in the Tokyo-Yokohama area, patients with progressive disease or who become refractory to treatment with conventional drugs should be removed from the area as quickly as possible. In addition, they should not be returned to the area since the disease usually returns and exhibits itself in a more severe form.

CONCLUSIONS

The practice of allergy in Japan is surprisingly similar to the practice of allergy in various areas of the Continental United States. The two problems mentioned: 1) lack of comprehensive survey of the allergens and, 2) T-Y asthma are the only significantly different problems. Many allergic patients who arrive in this area do very well, others continue to have their problem much as they did in the United States, and a few people are worse here than they were in the area from which they came. Many allergic children do surprisingly well here. The air pollution seems to have minimal effect on their basic allergic disease and I have yet to find a child with air pollution bronchitis. In some of the allergic asthmatics the air pollution is an aggravating factor of a non-specific nature different from the specific process seen in the patient with T-Y asthma.

Tokyo-Yokohama asthma in United States personnel persists as a problem. The symptoms and frequency of the disease has not changed from earlier reports and we have learned nothing new concerning its treatment or etiology. Lack of allergen surveys for the area handicap the allergist and forces one to fall back on knowledge and material brought from the United States. Despite this handicap allergy patients do as well or better on treatment here as in the United States.

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"It will be a sad thing for scientists if they fail to choose wisely and act energetically toward valuable and attainable goals – for, if they do not choose what they shall do, others will choose for them."

Pierce J.R. Editorial. *Science* 172:115, (9April) 1971

EXERCISE-INDUCED BRONCHOSPASM IN ASTHMATIC PATIENTS

MAJ R. M. Katz, MC*

Physical fitness and physical endurance are important standards of the Armed Forces, and yet there are some trainees who often complain of chest tightness or pain, cough, excessive fatigue, or wheezing after exertion. A significant proportion of these men have asthma and in some of them, exercise seems to be the only precipitating factor. This exercise-associated wheeze, often labelled exercise-induced bronchospasm (EIB) is a phenomenon which occurs during or after exercise. It has been reported in up to 100 percent of asthmatic patients when exercise is continued for more than five minutes, and it is not correlated with antigen exposure. It has been stated "A post-exercise fall in $FEV_{1.0}$ is so constant in the asthmatic that a failure to demonstrate it should lead to reconsideration of the diagnosis or technique of the test" /1/. Physical exercise by such a person has two distinct and opposite effects on his ventilatory function depending upon the duration and level of exercise /1,2/. Exercise lasting less than two minutes increases the forced expiratory volume in one second ($FEV_{1.0}$); whereas, exercise of longer duration produces a fall in $FEV_{1.0}$.

Exercise has been done with the stairway test /3/, walking /4/, a treadmill /5/, and cycling on the cycloergometer /6,7/. With the treadmill, work can be calculated from the incline (usually 10 percent) and belt speed (often three miles per hour) and the weight of the individual. However, many individuals cannot complete the six to ten minutes of exercise required to produce bronchospasm. Running up and down stairways to produce wheezing requires five to ten minutes. The work rate for this test also varies for each patient according to weight. Work done with level surface running varies with the patient's

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weight and distance traveled. Testing patients on the cycloergometer has the advantage of providing the exact amount of work intensity and is reproducible under standard conditions. /7,8/. A lack of standardization of work intensity made earlier observations of metabolic and physiologic changes during bronchospasm induction difficult to compare. Recently a study /8/ done with the cycloergometer elucidates the metabolic, physiologic and ventilatory relationships.

In a two-month study (Nov-Dec 1970) at Brooke General Hospital 32 patients who had given a history of atopic asthma were subjected to six minutes of maximum exercise on a treadmill with ten degrees inclination. Pulmonary function tests were performed at ten minutes post-exercise. Only seven patients revealed a 10 percent to 20 percent decrease in $FEV_{1.0}$ and another three patients revealed 20 percent or greater fall in $FEV_{1.0}$. These results differ from the early literature which dealt with asthmatic adults in which a greater percentage of patients revealed bronchospasm after exercise, /1,3/. Because allergy testing and physical examination may be nebulous, a more thorough evaluation is recommended in patients with a history of bronchospasm. A review of previous studies will elucidate this evaluation.

Protean postulates for the causes of exercise-induced bronchospasm have been suggested, and these include hypoxemia, metabolic acidosis, hypocapnia, activation of stretch reflexes, and release of aminoamines.

Hypoxemia, postulated as a cause of bronchoconstriction, is based upon the investigation of patients already in bronchospasm and then followed to the wheeze-free state. /4,6,9,10/ An uneven matching of alveolar ventilation to alveolar perfusion is suggested as present before bronchoconstriction is manifested. /11/ In early bronchospasm hyperventilation is common and this seems an unusual time for hypoxemia to manifest itself on the basis of airway obstruction. However, some support for hypoxemia is noted from low CO_2 tension associated with ventilation perfusion defects noted by radioactive xeon scanning in early stages of bronchospasm. /4,11/

Metabolic acidosis noted post-exercise has also been suggested as a cause of increased airway resistance in the asthmatic patient. /6,12/ The hydrogen ion concentration increases

during exercise and continues for ten to fifteen minutes after exercise. This is concomitant with a HCO_3 and a $PaCO_2$ fall. However, the findings have not been constant in the asthmatic patients studied under the limited conditions noted. In fact, it has also been shown that prolongation of exercise lowers the pH and is associated with increased vasoconstriction in normal individuals. /13/

Hypocapnia has been shown to produce regional bronchial narrowing. In one report /14/ studies were done before and after exercise with PaO_2, and $PaCO_2$, and $FEV_{1.0}$ measured as correlative factors. A fall in $FEV_{1.0}$ was associated with a change in $PaCO_2$ and hyperventilation. Rebreathing seven percent CO_2 diminished the induced bronchospasm suggesting hypocapnia as a precipitory factor in EIB. /14/ Hypocapnia resulting from hyperventilation has also been reported to increase airway resistance in normal patients. /15/ Another study /16/ showed no correlation with hypocapnia.

An altered reflex from the chest wall or altered "length-tension" relationship of the respiratory muscles has also been considered as a cause of bronchospasm. /4/ Hyperventilation alone is associated with significant reduction in bronchial tone. /17/ The induction of beta-adrenergic, alpha-adrenergic or cholinergic blockage has been shown to have no effect on exercise-induced bronchospasm in man. /14,18/ It is speculative that bronchoconstriction to hypocapnia depends upon the resting state of bronchial tone and atropine, which decreases muscle tone, reduces the size of the response to the given stimulus.

Recently, new evidence indicating little or no association of EIB with blood gas or ventilation abnormalities has been presented. /16/ In this study, serial arterial blood gas and ventilation studies were performed on atopic asthmatic children before, during, and following vatious work intensities. The onset of bronchospasm with changes in blood gas, alveolar gas, and metabolic relationship could not be correlated in these patients. Investigations were performed after a steady state was reached and then exercise (consisting of cycling at 60 rpm, starting with a work rate of 25 watts) for six minutes. Additional 25-watt work increments were imposed until the subjects were unable to maintain the work rate due to fatigue (heart rate usually greater than 180 beats per minute) or bronchospasm. Between each work increment a

ten-minute recovery period was allowed during which time PEFR and blood-gas analyses were obtained at two-minute intervals. These arterial blood sample collections were compared with samples taken before each work rate and during the sixth minute of exercise. Despite increased airway resistance in some patients, there was no correlation with the onset of bronchospasm to metabolic changes. Similar values for $PaCO_2$ throughout the investigation were noted for the children with bronchospasm and those without bronchospasm. Essentially patients with significant bronchospasm following exercise and those who do not develop significant bronchospasm upon exercise have similar blood-gas and alveolar-gas values.

Arterial-alveolar oxygen gradient changes were an early finding in those patients who subsequently developed EIB. In these patients, increased perfusion to the ventilated and non-ventilated regions would yield a higher gradient difference in non-ventilated areas. Thus, ventilation perfusion defects are early findings in subjects with bronchospasm induced by exercise. This occurrence could cause the symptom complex of chest tightness or pain, breathing difficulty, early fatigue and reflex coughing.

An observation that frequent repetitious periods of exercise (less than two hours apart) is followed by a progressive decrease in EIB in some asthmatic patients /13/ is consistent with the humoral agent as a probable cause for bronchospasm. Such agents may be an enzyme, or amino-amines such as histamine, slow reactive substance of anaphylaxis (SRS-A), bradykinin, serotonin (5 hydroxytryptamine) or a combination. /3/ It is possible that reactive hyperemia of exercise is of sufficient stimulus for histamine release. /3/ However, the failure of antihistamine to block EIB argues against it as a major factor involved. Serotonin has been given experimentally to asthmatics without resulting bronchoconstriction. Although it is also a potent bronchoconstricting agent, SRS-A remains unidentified chemically and no specific antagonist is known to block its possible effect. Therefore, it has not been possible to clearly eliminate SRS-A as a factor in exercise-induced bronchospasm. Bradykinin has been shown to be a stimulatory agent for decreasing the $FEV_{1.0}$ /19/; and Bradykinin is also released by an enzyme initiated by a rise in skin temperature and sweating, and is compatible with the onset of EIB. At the present time, there is no practical way to measure the in vivo

activity of bradykinin. Repetitious exercise is consistent with depletion of stores of a bronchoconstriction substance or an enzyme responsible for its release. Support for this theory is also noted in studies of decreased incidence of bronchospasm associated with exercise after the administration of disodiumcromoglycate. /20/ This compound has the property of blocking the liberation, but not the effects, of the mediators of tissue reaction in reagin-mediated anaphylactoid (Type 1) hypersensitivity.

The review of previous investigations of exercise-induced bronchospasm and our findings in young adults in the Armed Services reveals that approximately 30 to 50 percent of patients with atopic asthma can be shown to have EIB. Probably intolerance to exercise or specific work intensity causes wheezing rather than the converse. EIB can be reduced if exercise is limited to less than two or three minutes, and probably further reduced if repetition of the exercise occurs at less than two-hour intervals. Bronchodilator drugs consisting of oral ephedrine-theophylline-phenobarbital preparations or isoproterenol (0.32 mg) given two hours before exercise will often reduce or abolish the post-exercise bronchospasms.

The exercise test for the induction of bronchospasm can be useful in the evaluation of individuals with an atopic asthma history for Armed Services induction or enlistment. If bronchospasm occurs during or in 10-30 minutes post-exercise, the diagnosis of asthma can be documented. This test can also help in separation evaluations or in proper profile restrictions for the asthmatic patient.

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I cannot overstate my conviction, however, that the medical profession is at a major crossroads. Regardless of the methods we choose, we must learn to translate wishful thinking and languid philosophizing into purposeful action. We must stop yearning toward the past and look to the future, if we hope to preserve the noble traditions of our profession and add to the record of its great achievements.

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ALLERGENS AND ALLERGIES AT FORT HUACHUCA, ARIZONA

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Fort Huachuca is located in southeastern Arizona, approximately 70 miles from Tucson. It lies on the northeastern slopes of the Huachuca mountains with an elevation of approximately 5,000 feet. There are minor mountain ranges surrounding the area, with several peaks higher than 9,000 feet. The post has a population of 10,700 with 4,000 coming into the area during peak working hours.

Raymond W. Bliss Army Hospital operates 110 beds and serves a population of approximately 26,000; has an average hospital admission rate of 2,800 patients annually and its outpatient and specialty clinics accomodate 150,000 individuals each year.

Climate

The temperature at Ft Huachuca are relatively mild throughout the year. From data collected between 1956 and 1969, the mean average temperature in spring is 66 degrees; 76 degrees in the summer; 67 degrees in the fall and 48 degrees in the winter. Summer afternoon temperatures are kept down by the high frequency of cloudiness. Mid-day winter temperatures usually rise to a range between 55-65 degrees. Rarely does the temperature go below the freezing level.

The amount of precipitation varies with the seasons. In the spring, the average precipitation is 0.45 inches; 9.29 inches in summer; 2.56 inches in the fall and in the winter 1.96 inches. The spring season is usually sunny but also dry, windy and dusty. About three percent of the annual precipitation occurs during this season. The month of May has an average of 0.07 inches of precipitation. Numerous

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showers and thunderstorms occur throughout the summer months, usually in the afternoon or evening. More than 65 percent of the annual precipitation occurs during the summer season. The fall season accounts for about 18 percent of the annual precipitation; and the winter season approximately 14 percent. Abundance of sunshine, light wind and cool evening temperature characterize the fall season. Approximately one fifth of the winter precipitation occurs from snow which rarely stays on the ground except at elevation over 7,000 feet.

The relative humidity is usually lowest in May with an average of 23.8 percent and highest in August at 59.4 percent. Night time relative humidity is generally as much as 90 percent higher than day time humidity.

Gusty surface winds are frequent, especially during the fist six months of the year. Gusts of 40 mph and over are not uncommon from January to June, especially in April.

Aero-Allergen Survey

Aero-allergens in the Fort Huachaca area were surveyed by Mr. Wayne Johnson of the Environmental Science Services Administration Weather Bureau Office during the period between January 1, 1969 through December 31, 1969. The survey indicated that aero-allergens are varied and the area experiences only a short pollen-free period each year. The variety of pollens can be attributed to the location and elevation of the post which results in the flora being different from an area of a lower elevation. Some difference, therefore, is found between the aero-allergens in Fort Huachaca and Tucson area. The time and the degree of pollination is greatly affected by the temperature changes and the amount of water supply. At the foot of the mountains where the rainfall is greatest, varieties of trees not usually seen in the valleys are found.

Mountain cedar starts the pollen season in December and continues until February; followed by the juniper pollen which reaches its peak in March. Pollen from cottonwood, which grows along the river banks, starts around the middle of January and reaches its peak in February. Sycamore, Mesquite, oak, mulberry and ash are the other trees that pollinate in April and May.

The false ragweeds are common in the desert area. While most of them pollinate in the fall, rabbit bush, a franseria, sheds its pollens in March for about three weeks.

Among the grasses, bermuda appears to be the most serious offender in this area. Pollination starts in April and reaches its peak in August and September. Bermuda grass is widely used in landscaping all residential areas in the post. Furthermore, it seems capable of cross-reacting with some eastern grasses. Other grasses of minor importance are Johnson grass and rye grass.

The fall weeds are made up of the franserias, chenopods and amaranths. Slender ragweed, sagebrush, careless weed and Russian thistle are common and grow during the warm weather, shedding their pollens in August and September.

The different varieties of molds have been of minor importance in a dry area; however, during the entire year there were significant counts for several varieties--primarily Alternaria, Cladosporium, Helminthosporium, smut and rust.

Clinical Survey

Records of 204 patients presently receiving hyposensitizayion injections in the Allergy Clinic were reviewed. Thirty-seven percent of the patients started their allergy problems in Fort Huachuca while 63 percent started their allergy conditions elsewhere. There were 118 patients with hay fever, 32 with bronchial asthma and 39 with both bronchial asthma and hay fever, and 26 other allergic problems. Assessment of the immediate clinical response upon their move to this area was made. Of the group that started their allergy problems before their arrival in Fort Huachuca, 27 percent showed immediate improvement, 39 percent actually became worse and the condition of 30 percent remained the same. Among those that showed improvement, 43 percent had allergic rhinitis, 34 percent had bronchial asthma and 20 percent had both asthma and rhinitis and 3.0 percent had other allergic problems. Only 12 patients in the group had been advised or received compassionate transfer to Fort Huachuca because of their allergy condition.

CONCLUSIONS

A wide variety of aero-allergens are found in the Fort Huachuca area capable of allergic sensitization.

Atopic individuals with pollen sensitivity generally continue their symptoms and a significant number of asymptomatic atopic individuals develop initial symptoms upon moving to this area.

Patients with asthma, whose underlying problem is recurrent infections appear to respond favorably to this climate.

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FOOD SENSITIVITY AND MILITARY SERVICE

MAJ Gerald B. Goldstein, MC*

The diagnosis and treatment of food sensitivity has been a problem for many years. As the concept of allergy becomes increasingly popular among the lay population, foods as well as other allergens may be incriminated by the patient as causing any one of a number of symptoms, be they allergic in origin or not. The civilian doctor has a simple expedient in that he may eliminate the suspected food from the diet. The same avenue of approach, however, is not always tenable for the military physician whose patients often require immunizations and may be sent to area where special diets are not readily available. An example of the problem peculiar to the military was demonstrated by a young man seen at Tripler Hospital following medical evacuation from the Republic of Vietnam. Before induction he gave a history for delayed reactions to egg which had been documented several times by oral challenge. Although he passed his induction physical, enough credence was placed in this history to send him overseas without immunizations. In addition, provisions were made for him to live by himself so as to prepare his own diet. When the situation became known to the proper authorities, he was medically evacuated to Hawaii and eventually to CONUS. Although this was an isolated incident, it is still evident that much time, effort, and expense could have been saved had the significance of his history been appreciated in the first place. The Army clearly recognizes the problems related to food sensitivity and specifies that a bona fide history of a severe generalized reaction to common food is a cause for rejection for appointment, enlistment, or induction (AR 40-501, Chapter 2, paragraph 2-39a). Milk, eggs, beef, and pork are specifically mentioned, but the list could be expanded at the discretion of the examining physician to include other foods commonly found in the diet as well as certain spices, tenderizers, and dyes.

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DEFINITION OF TERMS; CLINICAL ASPECTS

Ideally, food allergy and food hypersensitivity are terms which should be restricted to situations in which typical atopic allergic symptoms are induced by the ingestion of a food or to situations in which other symptoms are repeatedly shown to be due to foods in which there are demonstrable immunologic reactions of a type believed to be etiologic in other forms of allergy. The physician is well aware of the immediate symptoms induced in sensitive individuals by the ingestion of certain foods such as shellfish, nuts, eggs, chocolate, and others. Indeed, these hypersensitivity reactions may be among the most serious encountered in clinical allergy and tend to occur no matter how infrequently the offending allergens are ingested. The severity of symptoms does not necessarily relate to the quantity of food partaken. Fortunately, food allergy of this nature is not common among the young population being inducted into military service.

Food sensitivity is a broad term, encompassing not only food allergy or food hypersensitivity, but certain other conditions in which there is a reproducible exaggerated or abnormal reaction to the ingestion of a specific food or foods. For example, certain infants develop iron deficiency anemia, or chronic occult gastrointestinal blood loss associated with milk ingestion; and do not grow and develop at normal rates. Various investigators have described precipitins to milk in the sera /1-3/ and stools /4,5/ of some of these children. Food sensitivity of this nature involves primarily infants and children and would not be a problem for the physician in screening inductees or treating active duty personnel. These observations are mentioned so as to illustrate that food sensitivity may appear as a chronic process with a number of unusual symptoms relating to any or all of the body systems.

As a result in gaps in our knowledge, "sensitivity" often overlaps with the term intolerance. The term food intolerance is preferable when an immunological etiology is unlikely. For example, if a nonimmunologic cause of celiac disease or idiopathic steatorrhea was established, the term gluten intolerance would be applicable. As another example, food intolerance may play a role in ulcerative colitis. Several workers /6-8/ have indicated certain foods may contribute to gastrointestinal symptoms in a number of subjects with this chronic disease, and have

recommended that clinical remission be sought by elimination of milk, fruits, and cereals from the diet. In many cases of food intolerance, clinical impressions have formed the basis for the reports; but a critical evaluation of past evidence plus further studies is necessary before immunological factors can be implicated in the pathogenesis.

The relationship of intestinal lactase deficiency to milk intolerance is another problem which merits consideration. Controlled studies by various investigators /9,10/ suggest an isolated hereditary lactase deficiency is prevalent among African Bantus and American Negroes. Certainly this diagnosis should be suspected with a history of chronic diarrhea and abdominal distention, especially if symptoms are exacerbated by milk ingestion. However, decreased small intestinal lactase activity does not necessarily imply a genetically controlled alactasia. Almost any condition predisposing to inflammatory changes in the intestine may result in a significant disaccharidase deficiency /11/, and the deficiency is often proved to be secondary only after normal enzyme activity returns following successful treatment of the basic disease.

PATHOGENESIS OF FOOD SENSITIVITY

The production of reagins to food proteins and their relationship to atopic symptoms has been recognized for some time, and clinical and immuno-chemical studies have been carried out to determine the nature of the particular food allergens responsible for stimulating skin-sensitizing antibody. For example, the simple chemical called chlorogenic acid has been found to stimulate skin-sensitizing antibodies in certain subjects sensitive to green coffee, oranges, castor bean, and several other fruits and vegetables. /12,13/. In another recent paper a subject with severe hypersensitivity to wheat gliadin was studied. It was found that the patient's serum contained skin-sensitizing antibody in a titer of 1:10,000 when passively sensitized volunteers were challenged with minute quantities of α-gliadin allergen. Reaginic activity was closely associated with serum IgE antibodies. /14,15/

Skin testing to foods is generally considered unreliable /16-21/ and the presence of a small quantity of reagin to a

specific food substance is not necessarily clinically significant. However, when a strongly positive skin test to a food in question is associated with immediate symptoms upon ingestion of the food, an etiologic relationship between the reagins and clinical sensitivity to the food may exist.

ROLE OF PRECIPITINS IN FOOD INTOLERANCE

A pathophysiologic role for either serum or stool precipitins to food proteins has not been established. Such antibodies could serve a protective function or they could be of pathogenic significance when they contact antigen in vivo by initiating a sequence of events leading to clinical symptoms. Some precipitins, on the other hand, may well be innocent bystanders arising as a secondary phenomenon as a result of specific defects in the enzymatic digestion of food proteins, At present the finding of precipitating antibodies in either serum or stool may be considered as no more than an ancillary aid to the physician who already suspects food sensitivity, especially when milk or wheat proteins are involved.

TREATMENT OF FOOD ALLERGY

Elimination of symptoms-inducing constituents of an offending food or foods from the diet constitutes the major method of treatment of food allergy at the present time. Once this has been accomplished, there may be some value in prescribing a diet which minimizes common food allergens while emphasizing foods which are less likely to be sensitizing. A satisfactory diet is one containing a variety of foods which are known to be well tolerated.

The therapeutic success of a diet requires attention to several factors.

⇒ Diagnosis and treatment of accompanying inhalant or contact allergy should proceed, if indicated, and ideally should precede initiation.

⇒ Results of diet therapy must be interpreted with caution if the diet is given during a period of infection or at the time of the year when offending pollens or spores are prevalent.

⇒ A diet devoid of a specific food must be tried for a period of at least one week and in some instances for as long as four weeks.

SUMMARY

Food sensitivity in the adult population is not a common problem, and in most cases can be handled by means of a judicious elimination diet. In the military, however, where immunization is mandatory and where a mobile soldier is a necessity, dietary therapy in most instances is untenable. Therefore, a good dietary history providing documented evidence for sensitivity to common foods should alert the military physician to the problems which may arise should the candidate be inducted into the service. For the physician caring for military dependents with suspected food sensitivity, the main concern is still indentification and the elimination of the allergenic foods.

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ADVERSE IMMUNIZATION REACTIONS

COL Joseph L. McGerity, MC

It is a command responsibility to determine the requirement for prophylactic immunization of the individual soldier. It is medical department responsibility to administer the vaccine, toxoid or other immunization material. This is a fine but important distinction of responsibility that the allergist or other medical officer should bear in mind when evaluating a patient. The medical officer is responsible for the determination of the medical need for a particular immunization and safety of administration of the material to the individual. The command is the determining authority as to fitness of that individual to serve under existing immunization status in any particular position or location. /1/

The danger associated with the use of these prophylactic agents must be recognized, minimized, and balanced against the possible benefits so that harm is not inflicted upon healthy individuals. However, it is difficult to obtain accurate information on many of the rare (but significant) problems associated with immunizations. The reports of adverse reactions are scattered through many journals in isolated case reports, buried in the archives of the military medical services, and only rarely collected in a source such as Sir Graham Wilson's book, The Hazards of Immunization. /2/

TERMINOLOGY

I prefer to limit the term allergy or hypersensitivity reactions to immunization to those events that are associated with symptoms, physical findings and laboratory data consistent with immunologic reactions classified as Type I, Type II, Type III or Type IV according to the schema introduced by Gell and Coombs. /3/ Sensitivity is a term which we apply to those incidents in which an immunological pathogenesis basis appears likely but is not demonstrable.

Sensitivity is also used to describe those adverse reactions that result from a defect in the immunological defenses of the patient. Intolerance is applied to those adverse events that do not appear to be associated with any action of the immunologic system. Much confusion still exists in the literature because of lack of definition of terms describing adverse reactions to immunizations and in this the situation is similar to that existing in the investigation of adverse reactions to food. /4/

An uncomfortable reaction may be a normal concominant of the administration of an immunizing agent. Wilson /2/ defines a simple reaction as one that is experienced in greater or lesser degree by the majority of persons receiving the vaccine, is attended by local and constitutional disturbance lasting (in the case of killed vaccines) not more than a few days, and causing no local destruction of tissue or general manifestations other than those common to a febrile illness. The transitory sore arm, malaise, and febrile reactions that frequently accompany the administration of typhoid vaccine or influenza vaccine are examples of this simple reaction. Frequently administration of an analgesic-antipyretic at the same time and six and twelve hours after the injection of the vaccine will abolish or minimize this reaction. We have found this simple procedure to be helpful. Since instituted at this hospital it has decreased significantly the number of patients referred for evaluation for adverse effects.

TOXICITY AND OTHER REACTIONS

The toxicity occurring with these simple reactions may be due to an inherent component of the organism (as in typhoid vaccine) or due to the organism, the medium in which it is suspended (as with influenza vaccine) or the combination. Attempts have been made to isolate specific, purified antigens from the organisms that would be immunogenic but not toxic. No vaccines of this type are commercially available. Recently zonal centrifuged preparations of influenza vaccine have become available on the commercial market in which many of the medium impurities appear to have been eliminated. We have found this material (Influenza Virus Vaccine, Bivalent, USP. Zonomune) to be useful.

In a few cases influenza vaccine administered subcutaneously

has repeatedly produced severe fever and malaise resulting in loss of work time. In these individuals intradermal administration of 0.1 cc of vaccine instead of injection of the larger subcutaneous volumes appears warranted. /5/ It should be noted that administration of influenza vaccine intradermally will often produce a wheal and flare reaction suggestive of anaphylactoid (Type I) sensitivity. In an unpublished 1968 study at Letterman General Hospital we found that the majority of normal individuals manifested such a skin reaction, but later they received full doses of the vaccine subcutaneously without adverse reaction.

Previously fluid typhoid vaccine could also be administered intracutaneously so as to prevent simple toxic reactions while still producing a significant anamnestic response to the O antigen. This vaccine is no longer commercially available and the new acetone killed and dried vaccine is not approved for intradermal administration.

The more serious complicated reactions involve suppuration or invasion with extraneous microorganisms resulting in abscess formation or ulceration with toxemia. They include reactions associated with serious toxin effects on the cardiovascular, nervous, or other systems. These episodes result from contamination of material through faulty production or faulty administration of the vaccine. The outstanding example of this in military history was the thousands of cases of hepatitis due to contamination that was associated with the administration of yellow fever vaccine to US Army personnel in 1942. /6/ In most episodes the "clustering" of these cases suggests the source of the adverse reaction.

As is well-known, faulty production of an attenuated organism such as occurred early in the history of oral polio immunization can result in serious adverse effects. /7/ The effect of such attenuated organisms on the fetus is debated, but in general such immunization is best withheld unless the life of the mother is threatened. /8,9/

Abnormal sensitivity of the patient may be due to deficiency of immunological or other defenses, eczema vaccinatum which is seen in association with breakdown of the skin defenses usually, but not always /10/ occurs in young children. It should be emphasized that it frequently occurs at a time when there is no visible rash. /2/ The need in the United States

for continuation of smallpox vaccination with its attendant complications has been debated in the recent literature. I do not recommend smallpox vaccination for children with atopic eczema (either active or quiescent) that are being followed in the allergy clinic at Letterman; nor do I feel that vaccination of members of their family is indicated as long as they remain in this country. I would recommend that the patient be excused from the innoculation requirements for foreign travel, but in some circumstances of foreign travel I have recommended that other family members be immunized in an attempt to establish a high level of "herd immunity".

It is frequently difficult to establish the cause of benign generalized vaccinia. Some hold that it is due to autoinnoculation (as in eczema vaccinatum) but others maintain that generalized vaccinia is the result of a viremia and effects perfectly healthy skin. Roseola vaccinatum may be confused with benign generalized vaccinia, but may be distinguished by the ability to blanch the lesions. /11/

Chronic progressive vaccinia is a severe illness that is frequently fatal, especially in infants. It is often, but not consistently associated with immunological deficiency of either or both the immunoglobulin or cellular systems. /12/ No live vaccine should be administered to a patient with immunological deficiency disease or to members of the patient's family. The allergist-immunologist or the oncologist should clearly outline the danger of such immunizations to the patient and his family. /13/ There may be some increased risk of unfavorable reaction from smallpox or other live vaccines in patients receiving long-term corticosteroids for any reason. /14/

Although abnormal sensitivity of the indivdual to a variety of immunizing agents may be manifested by various allergic reactions, not all of these can be classified by the English schema /3/ but attempts to do so will stimulate further research into these problems.

Type I reactions are classically demonstrated either by the immediate wheal and flare of the direct skin test or by passive transfer studies (Prausnitz-Kustner reactions) with the appropriate antigen. The techniques and necessary precautions to be observed in the use of the biological agents for skin testing has been very well presented in a recent technical bulletin /15/ and earlier by Colonel Robert E. Smith, USAF (MC) and his coauthor. /16/ It must be emphasized that many of the

immunizing materials are irritants or nonimmunologic histamine releasers when administered intradermally as full strength material and, because of this, may produce false positive reactions. Anyone responsible for the determination of sensitivity to these materials should become familiar with their intradermal reaction in a normal, nonsensitive, population, otherwise, many individuals will be falsely certified as allergic. This has been a problem at many training centers over the past several years, and as a result, the benefits of immunization are withheld from patients.

At the same time many patients have been told that they are allergic to certain agents without note of the basis for this impression being entered on their immunization record or in their health record. It is important that full particulars surrounding positive skin tests or adverse reactions be recorded. Despite all adequate precautions severe reactions of the anaphylactoid type are bound to occur occasionally during skin tests. In such cases it is wise to hospitalize the patient for overnight observation as delayed reactions appearing several hours after the patient has recovered from the initial shock are not uncommon.

Type II reactions (cytotoxic) have not been reported to be associated with routine immunizations.

Type III (Arthus or immune complex) reactions are probably rather frequent and manifested as local inflammation occurring 6-8 hours after injection and subsiding at twenty-four hours. The name "Arthus" reaction is applied to these reactions even though Arthus originally described a specific reaction (ulceration) in a specific organ (skin) of a specific animal (rabbit) to a specific material (serum) administered in a specific manner (on successive days). In current literature the term "Arthus type reaction" is applied to postulated immunological reactions appearing in skin (intradermal tests), subcutaneous or intramuscular tissue (vaccine reactions) or lung (allergic alveolitis) which characteristically have their onset six to eight hours after exposure to the foreign antigen and which are subsiding at twenty-four hours. At times these reactions overlap in the time sequence with the Type IV (cellular) reactions of delayed hypersensitivity.

It is a reasonable hypothesis that many of the severe local reactions to typhoid vaccine or to tetanus toxoid are

on the basis of immune complex formation with complement activation (with or without the formation of anaphylatoxin). In most cases where these reactions occur with tetanus toxoid the patient is found to have had high levels of tetanus antitoxin at the time of the injection. /17/ However, pathologic confirmation of the local deposition of immune complexes or complement at the site of the reaction is lacking.

Type IV reactions are commonly associated with the intradermal administration of many bacterial and fungal antigens and may be important in protection against viral infections. The appearance of the skin reaction is comparable to a tuberculin reaction with the peak of reaction occurring between 24 and 48 hours. Severe reactions may be associated with vesiculation and ulceration. These reactions are either uncommon with subcutaneous or intramuscular administration of vaccines or have not been noted. The potential for delayed reaction to the preservative material exists with several vaccines. /18/

REACTIONS TO SMALLPOX VACCINE

An immediate wheal and flare (Type I) reaction to smallpox vaccine prepared in chicken embryo (Lederle Smallpox Vaccine Avianized) has been reported in a patient sensitive to egg protein. /19/ No such reaction to the vaccine used by the military service which is prepared in calf lymph (smallpox vaccine, freeze dried), has been reported to my knowledge. However, such a reaction might occur in individuals sensitive to beef protein. The occurence of such a local reaction without systemic systems is no contraindication to further vaccination with the same material as the therapeutic vaccination is comparable with the safety of allergy skin testing.

Urticarial reactions occurring several days after smallpox vaccination have been reported. /20/ A cause-and-effect relationship appears probable, but immunological tests to confirm this have not been reported. Others have postulated that the urticaria was due to the material used for dressing the vaccination site.

A photosensitivity reaction secondary to smallpox vaccination has been reported several times /21/ and I observed an additional case in an adult in Buffalo in 1967. The morphologic characteristics of the skin lesions are suggestive of

delayed hypersensitivity reaction, but, again, immunologic confirmation is lacking.

REACTION TO CHOLERA VACCINE

While protection obtained with the use of the cholera vaccine is only relative /22/, the minimal side-effects when balanced against possible benefit justifies the continued administration of this material to those subject to duty in an endemic area. However, the requirement for cholera immunization for admission to the United States has recently been removed. /23/ While rare severe toxic reactions to cholera vaccine are mentioned by Wilson, /2/ I have not confirmed any allergic reaction to this material in the three and a half years that we have served as allergy consultants to the Oakland Army Base Port of Embarcation.

REACTION TO PLAGUE VACCINE

A recent report from the Allergy Service at Brooke General Hospital indicates that a small, but significant, number of individuals have allergic reactions associated with the receipt of plague vaccine. /24/ Most often this was an urticarial reaction, but in one case it was anaphylactoid. These reactions which have occurred with the initial or with the booster doses are considered by Reisman /24/ to be due to antigens of the plague bacillus itself rather than to trace amounts of the culture material which contains beef antigen. In about half the cases reagin could be demonstrated by positive direct skin tests and in some cases by positive passive transfer studies. Several of these patients where challenged with 0.2 ml booster doses as a diagnostic procedure. All provoked reactions were easily controlled with epinephrine or antihistamines. It has not been our policy at Letterman to recommend such diagnostic challenges. Rather, we have accepted a reliable history of an allergic type adverse reaction with or without a positive skin test to a 1:100 dilution of the vaccine as a contraindication to further administration of the material.

REACTION TO TYPHOID VACCINE

Typhoid vaccine was introduced into army medicine in 1911 and has a long history of producing local discomfort and even temporary incapacitation due to the fever, chills, headaches, myalgia, and malaise of a constitutional reaction in 10-20 percent of recipients. The O antigen of Salmonella typhi is its dominating toxic constituent, and it would appear difficult to produce a suitably antigenic material without including the O antigen. As previously mentioned these toxic effects are almost always controlled with the administration of aspirin. Experience with cortisone-antibiotic regimens in the therapy of typhoid fever would indicate that a short course of steroid therapy would control toxic episodes if necessary.

With the phenolized TAB vaccine previously available for typhoid immunization the severity of toxic episodes could be reduced by the intradermal administration of a smaller dose without diminishing the antibody response. /5/ With the new acetone killed and dried (AKD) vaccine intradermal administration is contraindicated.

Wilson /2/ describes eight cases of cardiovascular reactions suggestive of an anaphylactoid, Type I, reaction occurring in Royal Air Force recruits one to five hours after the administration of TAB vaccine. No such reactions to the new AKD vaccine have been reported.

REACTION TO INFLUENZA IMMUNIZATION

Each fall the annual influenza immunization program of the armed forces results in more referrals to the allergist than any other program. The influenza vaccine has an undeserved reputation for adverse reactions /25/ even among medical personnel. Most of the referrals result from a previous history of moderate to severe constitutional reactions to the influenza vaccine. In most cases the use of aspirin modifies such reactions and that is all that is necessary. An alternate approach is the administration of two doses of 0.1 ml of influenza vaccine intradermally two weeks apart. /5/ This appears to produce an adequate antibody response with very few constitutional reactions.

EGG SENSITIVITY REACTIONS

Because of experience with the typhus vaccine similiarly produced earlier in World War II physicians were warned about egg sensitivity reactions in patients receiving the influenza vaccine. In fact it was not, as it is not now, to be given to those who reported that they were sensitive to eggs or chicken. Incidentally, the number of so-called sensitives will vary widely depending on whether you phrase the question "ARE YOU ALLERGIC TO EGGS OR CHICKEN?" or "DO YOU EAT EGGS OR CHICKEN?"

No deaths were reported in the 1943 trials. In the larger, 8,000,000 dose trial of 1945 two anaphylactic deaths and one near death were reported to the War Department. I have reviewed those reported deaths. One clearly would fit the clinical criteria and postmortem findings associated with this diagnosis. The record of the other death is incomplete. Since those original reports only one additional death associated with the administration of influenza vaccine has been reported and it is not clear from the report that this was truly a hypersensitivity reaction. In any event it was not classical anaphylaxis. There have been many reports of the occurrence of nonfatal immediate hypersensitivity reactions — urticaria, bronchial spasm, shock, angioedema or laryngeal edema. While at one time some of these were attributed to a small amount of penicillin in the vaccine (not proven at the time and penicillin no longer in the vaccine) or to silk particles resulting from a step in purification (proven reaction, but a purification method since abandoned) the reactions have usually been attributed to the egg protein. The amount of egg present has varied from manufacturer to manufacturer and even between lots from the same source.

EGG PROTEIN SENSITIVITY

The usual questioning is sufficient to weed out those highly reactive to egg protein. There are only two injected vaccines containing egg in routine use for the active duty military at the present time. These are influenza vaccine and yellow fever vaccine. Neither are required for travel or duty in RVN and therefore from the viewpoint of the individual and from the immunization level of the army as a whole it is no problem to excuse a reasonable number from receiving these vaccines.

It has been demonstrated in both a civilian setting in Michigan and in military reports from Japan that when 86 percent of the school population or 80 percent of a military unit is vaccinated, "herd immunity" affords the unvaccinated remainder of the group a significant degree of protection. /25/ Thus less than 100 percent coverage will raise the immunity of a population in most diseases in which only a human reservoir exists.

Approximately one percent of the childhood population has dermal sensitivity to egg protein. Figures on the military group are not available but would not be expected to be higher. In allergic groups of children the incidence is 10-20 percent. In allergic children only 25 percent of those with positive skin tests have clinical allergy to the egg protein. As they grow older they tend to lose the clinical sensitivity while retaining the dermal sensitivity. /26/

Therefore in a group of adults with a past history, but no current history of allergy to ingestion of eggs, we might expect to find a large proportion of individuals with positive skin tests to eggs but only a small number of these would have an adverse allergic reaction to influenza vaccine. Letterman is not the setting in which to test this theory, but it has been tested in children on at least two occasions. Ratner and the group at NYU /27/ did it with influenza vaccine many years ago and more recently Kamin et al /28/ in San Antonio administered live attenuated measles vaccine to egg sensitive children. In the New York study there were a few adverse reactions (one to a test dose of 0.02 ID of influenza vaccine was severe). No adverse reactions were reported with the measles vaccine.

It is our policy to skin test with egg protein an individual referred for evaluation of possible egg allergy. If a positive skin test is obtained no vaccine is administered. If the skin test to egg and to a 1:100 dose of the vaccine is negative the egg-containing vaccine is administered in increasing dosage under constant observation.

YELLOW FEVER VACCINE

Over 34,000,000 doses of yellow fever vaccine have been distributed. With the current material less than 10 percent of the vaccines have any constitutional symptoms and no significant

loss of duty time occurs. The vaccine is prepared in egg material, and those individuals who are unable to eat eggs or chicken should not receive this vaccine.

TETNUS TOXOID

While tetanus toxoid does not give perfect protection it is one of the best immunizing agents available and one of the least toxic. The lack of her immunity and the severity of the disease (still fatal in 60 percent of cases) makes the inability to receive this vaccine a serious liability to the individual. Therefore, every effort should be made to confirm or to rule out a sensitivity to tetanus toxoid.

Since certain of the peptones and silk antigens present in early preparations have been eliminated reports of anaphylactic reactions have been rare /29/ although local reactions to the alum precipitated material are fairly common. These reactions are suggestive of an Arthus type III reaction. Use of the alum precipitated tetanus diphtheria toxoid (T-d) for skin testing will produce a wheal and flare in most individuals and for this reason we use dilutions of the fluid toxoid for the skin testing. A positive reaction with 0.02 ml of a dilution of 1:100 or greater is considered a contraindication to further administration of the material at that time. It is our policy to then submit a blood sample from the patient to the National Communicable Disease Center in Georgia. We have been gratified to find in almost all cases that these individuals have an antibody level well above the minimal protective limit of 0.01 mouse units. /17/ Our advice as to the necessity of future boosters or need for use of human tetanus antitoxin in case of injury is based on our extrapolation from the charts of antibody persistence. /30/ In some cases it is evident that no routine booster will be required for several years and by that time the reagin level may have declined.

EVALUATION OF PATIENT *"for possible hypersensitivity to an immunizing agent"*

If asked to evaluate a patient for possible hypersensitivity to an immunizing agent the physician should determine the extent of his evaluation and the risk to which he is willing to subject the patient during such evaluation. He

should weigh several factors (1) The nature and history of the reported sensitivity, the availability of alternate methods of prevention, the disability likely to be associated with the particular disease in the particular patient, (2) the availability of adequate therapy for the disease, and (3) the possible inconvenience to the patient and administrative disturbance that will be produced if the individual remains unimmunized.

If hypersensitivity is confirmed possible dosage modification or change of route of administration should be considered. In many toxic or Type III reactions it is evident that adverse reactions are dose related, and adequate protection may be obtained by decreasing the dose to tolerable level. Intradermal administration may be substituted for subcutaneous administration in certain cases.

In most medical facilities the allergist will be consulted about procedures, dosages, routes of administration, possibility of future reactions and new developments in the field of vaccine prophylaxis even though it is evident that many of the adverse reactions have no immunological basis. As indications for specific agents and the agents themselves change, the allergist must remain informed if he is to evaluate properly and recommend for the patient. Education of the military physician as to the significance of adverse reactions and the cautious interpretation of skin tests will prevent unnecessary consultations and administrative problems.

"Immunization is promoted today, as always, with dedication and passion. No matter how firm the scientific foundation of each newly developed vaccine, immunization itself is carried out with some of the fervor usually characteristic of religious zeal." /31/ Many other observers are disturbed by the possible danger of hyperimmunization because the spectre of vasculitis /32/ or amyloidosis /33/ is always in the background. It may well be the function of the allergist to maintain a position near the center of these opposing views of immunization as his training and experience should enable him to chart an accurate course through the immunological currents.

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MALARIAL ANTIBODY

CPT Carroll W. Cederburg, MC

Despite widespread control and eradication campaigns, over one billion people, more than one-third of the world population, are exposed to malaria infection. /1/ For several hundred years the advanced countries of the world have been from non-tropical areas. They were confronted with the problem of malaria primarily when their troops moved into endemic areas. Malaria has always been an enemy of the military. During World War II in the South Pacific malaria caused five times as many casualties as did combat (Schneider, 1962).

For members of the American Armed Forces the present primary malarial problem is drug-resistant falciparum malaria. This variety of the disease produces the greatest mortality and morbidity. Drug resistance has been noted since World War II but it has not been considered significant (Fairly, 1946). During the Korean conflict in the 1950s Plasmodium vivax (P. vivax) was prevalent, and so malarial drug resistance was not evident as the problem. With American involvement in Vietnam reports of drug resistant malaria became frequent (WHO, 1964). Drug resistant malaria has also been reported in Malaya, Cambodia, Laos and Thailand (Tigertt, 1966). The actual incidence of resistant falciparum malaria is not known but is common. During 1965 the number of soldiers evacuated from Republic of Vietnam because of malaria equaled those evacuated because of battle wounds (Tigertt, 1966).

Although therapy has succeeded in greatly reducing the mortality and morbidity of malaria; this, however, is extremely inefficient, temporary, costly, and inadequate. Recent attention in malaria research has been focusing on the human immunologic system.

METHODS

As early as 1907 attempts had been made to detect

malarial antibody (DeBlasi, 1907). Gasbarrini in 1913 was able to demonstrate positive complement fixation tests in 24 out of 28 malaria patients. In 1918 Pewny was able to demonstrate positive precipitins with blood from malaria patients. In 1938 Eaton reported on the agglutination of P. knowlesi by immune serum. Hemagglutination techniques including indirect methods were recently described by Stein and Desowitz (in 1963). In 1961 the fluorescent antibody technique was first used successfully by Tobie and Coatney.

The indirect hemagglutination test (I.H.A.) is conducted with human group O erythrocytes that have been tanned and then sensitized with malarial antigen. With only one drop of blood on filter paper, the I.H.A. test can detect minute amounts of antibody. Titers greater than 16 are indicative of past or present infection. /2/ Specificity at titers greater than 16 is over 95 percent. The I.H.A. test does not differentiate between the various types of malaria. Antibody response occurs in man 6 - 10 days after infection and may be detected up to fourteen years after cure. /3/ Irradication of malaria in Tobago in 1954 served as an excellent source of serum for studying the persistence of malarial antibody. Although antibody could be detected up to fifteen years after infection, the antibody level usually fell to negligible levels by 6 - 12 months. /3/

The indirect fluorescent antibody (I.F.A.) technique is more sensitive and specific than the I.H.A. test and it is capable of identifying the different species of Plasmodium. /2/ Titers of greater than 16 are considered diagnostic. I.F.A. titers peak by 8 - 10 weeks (usually 1 - 2 weeks) and decrease to a mean of 9 six months after infection and treatment. /4/ Fisher /5/ studied the effects of repeated infection with P. vivax in American soldiers in Vietnam. The titer was unrelated to the number of repeated infections. He also observed that patients with relapses had no significant difference in their I.F.A. titers when compared to those patients with single or repeated infections.

With good serologic methods available there is now opportunity to study more completely the epidemiology of malaria and its response to treatment. In rare selected cases, the I.F.A. can be of diagnostic value.

One of the prime movers for the study of malarial immunology is the hope for the development of a malaria

vaccine. In view of the persistence, relapsability and repeated individual infections of malaria, the question remains -- is there a protective antibody and is it significant?

In 1910 Etienne and Edmond Sergent reported partial protection from malaria in canaries following immunization with killed sporozoites. In 1917 Soteriades reported clinical improvement in a patient with acute malaria following injection with 10 cc of serum obtained from a patient with chronic malaria. Several subsequent studies in man and animals confirmed the presence of effective transferable passive immunity (Coggeshall, 1937; Manwell, 1949). Passive immunity apparently does play some role in the protection of newborn African infants from malaria. Studies show high resistance to malaria in neonates born of women with chronic malaria. /6/ Active immunization against malaria in animals, primarily monkeys, has provided further evidence for the presence of protective malaria antibody. /7, 8/

Most people in endemic malarial areas have elevated gamma globulins (Garnham, 1963). Often Immune globulin E (I.g.E.) was elevated in malaria as well as in other parasitic infections; this led to speculation that IgE contained possiole protective antimalarial antibody (Catty, 1969). Subsequent studies have not demonstrated any protective antibody in the IgE fractions. /9/ I.F.A. titers and I.H.A. titers as well as the quantity of IgG and IgM have no correlation with protective immunity. /8/ Apparently much antimalarial immunoglobulin has no protective effect against plasmodial infection. In most animal species malarial immunity becomes manifest slowly only after prolonged persistent infection.

Advances towards malarial vaccine

Within the past year two major advances have occurred in malarial immunology. These have been the fractionation of specific malarial antibody and the isolation of a purified plasmodial fraction capable of inducing protective malarial antibodies in vivo. /10/ These two advances are basic to the production of a possible malaria vaccine. Silverman /10/ prepared several plasmodial antigens by protein fractionation. The various fractions were then injected into mice and in 15 weeks the mice were challenged with live plasmodia of the same strain; survival and parisatemia were recorded. Two of the various fractions induced immunity. Twenty-two out of

25 mice which received these fractions survived, whereas 50 out of 55 who did not receive these fractions died.

In 1969 Cohen et al /11/ introduced an in vitro method of testing malarial antibody. They used the parasite P. knowlesi which has a 24-hour growth cycle and which produces 6 - 16 merozoites per schizont. For their studies it was therefore necessary to achieve 24-hour growth rates of at least six-fold. Leucine was incorporated into developing parasites, and labeled ^{3}H-leucine in the media was measured to plot growth curves. Subsequent studies demonstrated the effect of varying doses of immunoglobulin on parasite growth. /11, 12/ Using this method of measuring malarial antibody activity, Cohen and Butcher /9/ then isolated various fractions of immunoglobulins from sensitized monkeys. No antimalarial activity could be demonstrated in IgA or IgE fractions. By preparing various fractions of IgG and IgM, they were able to detect protective antibody in both fractions. These fractions had no detectable effect on intracellular growth of parasites but did produce complete suppression of successive parasitic growth. In further studying protective antibody, these investigators found that its effect is not complement dependent, that bivalence is essential and that only the Fab fragments are active. Although the exact mechanism of action of protective antibody is unknown, the free parasites have been noted to agglutinate and fail to penetrate red blood cells in the presence of immune serum. Many of these properties are identical to those of viral neutralizing antibodies.

Association of malaria and other diseases

Other than direct antibody production there are other immunologic aspects of malaria. In 1963 epidemiologic studies revealed an association between malaria and the nephrotic syndrome in African children (Hendrickse, 1963). The main association was that plasmodium malaria reaches its peak incidence at the age of five when the childhood nephrotic syndrome also reaches its peak. This nethrotic syndrome was somewhat unique because steroids were either ineffective or harmful in the majority of patients. /13/ Soothill performed differential protein clearances on the children. He found Nigerian children had primarily the "dog-leg" type proteinuria

and that the IgG/ablumen clearance ratio provided the most significant means of separating the two types of nephrotic syndrome. In the so-called "malaria nephrotic syndrome," the ratio was higher.

Evidence that this nephrotic syndrome existed secondary to malaria was primarily speculative until 1969 when Ward /14/ demonstrated glomerular deposits of antimalarial IgM by immunofluorescent technique. He was able to demonstrate positive results in 3 of 12 cases and speculated that negativity in the other 9 cases might have been due to antibody excess /15/ or antigenic variation (strain specificity). In 1970 Voller /16/ added more supportive evidence by correlating high malarial antibody titers with high serum IgM levels in Ugandans who had the nephrotic syndrome. There now appears ample evidence that immune complex nephritis does occur secondary to some P. malaria infections. This nephritis is not steroid responsive in contrast to the usual European-American childhood nephritis.

Recent attention has been given to the relationships between malarial infection and autoimmune disease and Burkitt's lymphoma. In 1968 immunologic changes observed in normal population in Africa were thought to be secondary to repeated parasitic infections (Garnham, 1963). Consideration of this in conjunction with the rarity of autoimmune disease in Africa suggested a possible protective effect of parasitic infection. To test this hypothesis Greenwood et al /17/ in 1970 studied the effects of malaria infection on NZB and B/W mice strains. B/W mice are an experimental strain of mice who all develop positive antinuclear antibody (ANA) glomerulonephritis with the nephrotic syndrome by age 6 - 8 months and 97 percent die of renal failure by the age of 11 months. NZB strain mice develop a Combs' positive hemolytic anemia in over 90 percent of mice by the age of nine months. Greenwood et al /17/ in controlled studies then demonstrated almost complete protection against the development of the nephrotic syndrome in B/W mice by infection with P. bergheii yoelii. In NZB mice infection with P. bergheii yoelii significantly decreased and delayed the onset of hemolytic anemia. The reason for this apparent protective effect of malaria infection is obscure. Latent slow viruses play a role in the autoimmune diseases of NZB and B/W mice but apparently interferon stimulation by malaria is not responsible for the observed protection. /17/

The combination of virus and persistent malarial infection has also been recently investigated in Burkitt's lymphoma. /18/ Initial attention in this area was brought about by Dalldorf et al in 1964 who commented on the association of malaria with lymphomas. Interest was revived in 1969 when Burkitt himself /19/ reviewed the subject. Epidemiologic evidence incriminating malaria as a contributing etiologic factor in Burkitt's lymphoma is now beyond dispute. Burkitt himself postulates a combination of malaria and virus as being etiologic in this lymphoma. Subsequent studies published in 1968 by Jerusalem reveal the development of morphologically similar lymphomas in mice repeatedly infected with P. berghei.

COMMENT

Several unanswered questions persist. Why doesn't repeated and chronic infection with malaria confer immunity? What is the role of cellular immunity in malaria? What is the relationship between malaria and autoimmune disease and tumors? Would development of a malaria vaccine only alleviate acute erythrocytic malaria and in the process yield to the development of a parasite-host symbiosis where the gametocyte remains? Does protective immunity other than that directed against the merozoite exist?

The lack of development of protective immunity may be because the merozoite is only extracellular for less than one-half hour and thus yields little time for antigen recognition or antibody action. /26/

It has not been suggested but would be intriguing to speculate that low malaria morbidity and mortality in thalassemia and sickle-cell disease are the result of increased protective immunity brought about by increased exposure time of the merozoite with the humoral system. In view of the recent work by Cohen and his group /26, 28-30/ it would be interesting to see if sickle-cell patients with malaria do indeed have higher protective antibody levels.

There are many intriguing, pertinent, and valuable aspects to research in malaria immunology. A protective antibody does exist along with a now detectable stimulating antigen. Immunologic alterations in malaria may provide a clue for advances in autoimmune disease and tumor research.

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To make one final assumption, I am convinced that the new trends in public policy cannot be diverted or reversed, and that they will bring about profound changes in our patterns of practice. If that is true, we must modify those that are unfavorable when we can, adapt to them when we can't, but, above all, we must lead rather than be dragged.

Ilmler, G. Shattuck Lecture The anatomy of our melancholy. *New Eng J Med* 284:1406-1413, (24 June) 1971

APPENDIX I

EXCERPTS FROM ARMY REGULATION 40-501, Chapter 2
Medical Fitness Standards for Appointment, Enlistment and Induction into the Military Service (any branch)

The following "allergic" conditions are causes for rejection for military service at the present time.

Section XIII. Para 2-26

b. Bronchial Asthma, except for childhood asthma with a trustworthy history of freedom from symptoms since the 12th birthday.

Section XIV. Para 2-28

a. Allergic Manifestations

(1) Chronic Atrophic Rhinitis
(2) Hay Fever, if severe; or if not controllable by antihistamines or by desensitization, or both.

Section XVII. Para 2-35

o. Atopic Dermatitis. With active or residual lesions in characteristic areas (face and neck, antecubital and popliteal fossae, occasionally wrist and hands), or documented history thereof.
w. Urticaria, Chronic

Section XIV. Para 2-39.

a. Allergic Manifestations

(1) Allergic Rhinitis (see paragraph 2-28)
(2) Asthma (see paragraph 2-26b)
(3) Allergic Dermatoses (see paragraph 2-35)
(4) Visceral, abdominal and cerebral allergy, if severe or not responsive to treatment
(5) Bonafide history of moderate or severe generalized (as opposed to local) allergic reaction to insect bites or stings.
Bonafide history of severe generalized reaction to common foods, e.g. milk, eggs, beef and pork.

APPENDIX II

EXCERPTS FROM ARMY REGULATIONS 40-501, Chapter 3
Retention Medical Fitness Standards

Every one of the "allergic" conditions listed below normally renders a member unfit for further military service.

Section XII. Para 3-25

a. Bronchial asthma. Associated with emphysema of sufficient severity to interfere with the satisfactory performance of duty, or with frequent attacks controlled only by continuing corticosteroid therapy, or with frequent attacks not controlled by other oral medication.

Section XIII. Para 3-27

d. Rhinitis. Atrophic rhinitis characterized by bilateral atrophy of nasal mucous membranes with severe crusting, concomitant severe headaches, and foul, fetid odor.

e. Sinusitis. Severe, chronic sinusitis which is suppurative, complicated by polyps, and which does not respond to treatment.

Section XVI. Para 3-33

b. Atopic dermatitis. More than moderate or requiring periodic hospitalization.

ac. Urticaria. Chronic, severe, and not amenable to treatment.

Section XVIII. Para 3-36

a. Allergic manifestations.

(1) Allergic rhinitis. See paragraphs 3-27d and e.
(2) Asthma. See paragraph 3-25a.
(3) Allergic dermatoses. See paragraph 3-33.

EXCERPTS FROM AR 40-501, Chap. 3 Retention Standards

(4) Visceral, abdominal, or cerebral allergy. Severe or not responsive to therapy.

c. Miscellaneous conditions and defects. Conditions and defects, individually or in combination if -

(1) The individual is precluded from a reasonable fulfillment of the purpose of his employment in the military service, or
(2) The individual's health or well-being would be compromised if he were to remain in the military service, or
(3) The individual's retention in the military service would prejudice the best interest of the Government.

Questionable cases including those involving latent impairment and/or those when no single impairment but a combination of two or more impairments may be considered to render the individual unfit will be referred to physical evaluation boards for a determination of fitness.

d. Exceptionally, as regards members of the National Guard of the United States and the Army Reserve, not on active duty, medical conditions and physical defects of a progressive nature approaching the level of severity described as unfitting in other parts of this chapter, when unfitness within a short time may be expected.

6275 Smell, loss of sense of, complete 10

Hyperesthetic Rhinitis, allergic or non allergic. Not ratable unless complicated by loss of sense of smell or by chronic sinusitis.

6510-6514 Sinusitis,..., Chronic

Postoperative, following radical operation...	50
Severe, with frequently incapacitating recurrences..	30
Moderate with discharge or crusting or scabbing, infrequent headaches	10
X-ray manifestations only, symptoms mild or occasional	0

6602 Asthma, bronchial

Pronounced; marked emphysema, attacks very frequent, dyspnea on slight exertion, between attacks, marked loss of weight or other evidence of severe impairment of general health 100

Severe; moderate emphysema, frequent attacks (one or more weekly), marked dyspnea on exertion between attacks, impairment in general health manifested by malnutrition, etc. 60

Moderate; slight to moderate emphysema, attacks rather frequent (10-14 day intervals), moderate dyspnea on exertion between attacks 30

Mild; without emphysema, and occurring at widely separate intervals. 10

Emphysema

No separate rating; covered by this basic condition.

ABSTRACTS FROM VA SCHEDULE . . .

7118 Angioneurotic edema

Severe; frequent attacks with severe manifestations and prolonged duration	40
Moderate; frequent attacks of moderate extent and duration	20
Mild; infrequent attacks of slight extent and duration	10

7806 Eczema

With ulceration or extensive exfoliation or crusting, and systemic or nervous manifestations, or exceptionally repugnant	50
Exudation or itching constant, extensive lesions, or marked disfigurement	30
As below, if involving an exposed surface or extensive area	10
Slight; if any exfoliation, exudation, or itching, if on a nonexposed surface or small area	0